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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,366	09/19/2003	Fen Huang	34506.143	8954

25005 7590 08/27/2007

DEWITT ROSS & STEVENS S.C.
8000 EXCELSIOR DR
SUITE 401
MADISON, WI 53717-1914

EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
08/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/666,366	Applicant(s) HUANG ET AL.	
	Examiner Richard G. Hutson	Art Unit 1652	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 09 August 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 5 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: 1-45.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit: 1652

Continuation of 3. NOTE:

Continuation of 5. Applicant's reply has overcome the following rejection(s): The 102 rejection and the rejection under 112 first paragraph for new matter has been withdrawn as a result of applicants amendment of the recited temperature of at least 90oC..

Continuation of 11. does NOT place the application in condition for allowance because:
Claims 1, 4, 5, 7-10, 13-18, 21, 22, remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.
Applicants continue to traverse the rejection on a number of different basis. Applicants submit that they are not claiming all RNAse inhibitor proteins, but rather methods of use of the Rnase inhibitor proteins and the guidelines for such require a more all-encompassing approach, such that any description of sufficient, relevant, identifying characteristics may be sufficient.
Applicant's complete argument is acknowledged and has been carefully considered, however, is found nonpersuasive for the reasons previously made of record and repeated herein. Applicants assertion that the shared important structural feature of the referenced RNase inhibitor proteins is that they are proteins is not a convincing argument. As pointed out each of the referenced RNase inhibitors must be a protein, however, this remains an incredibly broad structural genus with respect to the claimed function of RNase inhibition, and even more so when the claimed proteins must maintain this RNase inhibition function in the presence of and thereafter at least 90oC heat. Further applicants are reminded that in addition to the above functions, such a claimed combination must achieve that "RNA present in the mixture or subsequently added to the mixture is protected from enzymatic degradation by Rnases".
As previously stated, the specification fails to describe additional representative species of RNAase inhibitor proteins and their claimed methods by any identifying structural characteristics or properties necessary to ensure the successful use of these inhibitor proteins, i.e. the combination of the RNase inhibitor protein and the specifically recited temperature conditions. Given this lack of additional representative species as encompassed by the claims, and lack of structural to functional characterization, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention.
Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 4, 5, 7-10, 13-18, 21, 22 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed methods of use of rat or human RNAsin, does not reasonably provide enablement for the claimed methods of use of any RNAase inhibitor protein in combination with the specified temperature and having the specified results. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.
As above applicants continue to traverse the rejection on a number of different basis. Applicants continue to argue that the person of ordinary skill in the art can be completely and utterly and totally ignorant of the structure of the RNase inhibitor protein and still be fully capable of practicing the invention as broadly as it is claimed, as applicants do not have to have knowledge of how an invention functions, merely that it works.
Applicants submit that the previous rather lengthy discussion of structure/function relationships, knowledge and guidance of which amino acids in the protein's sequence are critical to the desired function is irrelevant to the issue of enablement, as the person of ordinary skill in the art need only buy a commercially available RNase inhibitor, as knowledge of how an invention functions is irrelevant.
Applicants argument is not fond persuasive because it continues that methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan while producing variants as claimed by applicants (i.e., encoding a Rnae inhibitor protein) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without effecting the desired activity(i.e. RNase inhibitor activity in the presence of and thereafter a temperature of 50oC/90oC); (B) the general tolerance of any RNAse inhibitor protein to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of any RNAase inhibitor protein with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the necessary activity for the claimed methods and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not, it would require undue experimentation for one skilled in the art to arrive at the majority of those methods of the claimed genus having the desired result.
Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including those methods of use of any RNase inhibitor protein of variant thereof in combination with a temperature of at least 90oC. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988)..